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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/372,036	08/11/1999	PETER SCHUBERT	MERCK1694D2	9962

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EXAMINER

BASKAR, PADMAVATHI

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 05/31/2002

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/372,036	Applicant(s) SCHUBERT ET AL.	
	Examiner Padmavathi v Baskar	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 March 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 39-70 is/are pending in the application.
- 4a) Of the above claim(s) 39-41 and 44-49 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 42-43 and 50-70 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 39-70 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other:

Response to Amendment

1. The amendment filed on 3/5/02 has been entered into the record. Claims 42 and 43 have been amended and new claims 63-70 have been added. Claims 39-70 are pending in the application. Claims 42-43 and 50-70 are under examination as an elected invention (i.e., antibodies).
2. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Rejections Maintained

3. Claims 42,43, 50-59, 61 and newly added claims 63-64, 66-67 are rejected under 35U.S.C. (102 b) as being anticipated by Kohler et al 1990 (Infection and Immunity, 58, 1943-1950). This rejection is maintained for essentially the same reasons as set forth in the previous office action.

Claims are directed to an isolated antibody which specifically binds to the p60 protein from pathogenic *Listeria*, wherein said antibody binds an epitope from only one of the peptide, SEQ.ID.NO: 17, 20, 26, 29, 30 or 31 and said antibody obtained by immunizing said peptides.

Kohler et al 1990 disclose anti-p60 antiserum raised against purified p60 *Listeria* protein in rabbits. This antibody binds to p60 of *Listeria* (Fig 1) wild type and or recombinant p60. In the absence of evidence to the contrary the disclosed prior art antibody binds to any one of the peptides, SEQ.ID.NO: 17, 20, 26, 29, 30 or 31. Since the Office does not have the facilities for examining and comparing applicants' antibody and antibody of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed antibody and antibody of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594. Further, the antibody disclosed by Kohler specifically binds to *Listeria* and does not bind to other organisms such as *E.coli* (see figure 1 B, line 1). The prior art anticipated the claimed invention.

Applicants' arguments filed on 3/5/02 have been fully considered but they are not deemed to be persuasive.

Art Unit: 1645

Applicant argues that Kohler's antisera contain mixture of antibodies and does not anticipate the claimed invention. It is the examiner's position that the claims do not recite such limitations and applicant is arguing the limitations which are not set forth in the claims. If applicant intends to mean that the monoclonal antibodies specifically bind to an epitope from the group consisting of SEQ.ID.NO: 17, 20---, then the claims should recite such limitations.

The antibody recited in the prior art binds specifically to the p60 protein as shown in figure 1. It is clear that the antibody binds to the claimed epitopes since the recombinant protein containing PVAPTQ (see Figure 2, NA 859-924 encoding PVAPTQ (SEQ.ID.NO: 17) reacted with the antisera (see figure 1, B, lanes 2-3). Further, the immunogenic conjugate as recited in the claim 43 is disclosed by the prior art (see, page 1944, right column, under preparation of anti-p60 antisera). The immunogenic conjugate comprises purified p60 protein and Freund complete adjuvant. Further, the antibody disclosed by Kohler et al specifically binds to *Listeria* and does not bind to other organisms such as *E.coli* (see figure 1 B, line 1). The prior art anticipated the claimed invention and therefore, this rejection is maintained.

4 Claims 60, 62 and newly added claims 65, 68-70 are rejected 35U.S.C. (103 a) as being unpatentable over Kohler et al 1990 (*Infection and Immunity*, 58, 1943-1950) in view of Lerner (*Adv. Immunol* 1984, 136; 1-44) or Harlow and Lane 1988 (*Antibodies*; Cold Spring Harbor) as set forth in the previous office action.

Kohler et al 1990 teach a recombinant *Listeria monocytogenes* p60 protein and an isolated antibody that binds to p60 protein (abstract, Fig 3). Further, the antisera recognized the truncated p60 derivatives that indicate the antibody binds to different regions (i.e., epitopes) within the p60 protein (page 1945, left column and figure 2A). However, the prior art does not teach raising monoclonal antibodies against peptides of p60.

Lerner teaches various sets of antibodies required to track distinct regions of a protein (pages 11 and 12). Therefore, it would have been obvious to a person of ordinary skill in the art

Art Unit: 1645

at the time the invention was made to make monoclonal antibodies to different regions of p60 protein with a reasonable expectation of success because Lerner teaches that different antibodies are needed to track different regions of a protein.

An artisan of ordinary skills would have been motivated in applying the art disclosed by Kohler to Lerner to make different antibodies including the monoclonal antibodies to different epitope of p60 protein because it would have helped to distinguish different *Listeria* species. The motivation to do this comes from both Kohler and Lerner because Kohler teaches specific regions within p60 are important to detect *L.monocytogenes* among other species (abstract) and Lerner teaches various antibodies are required to track different regions of a protein. One of ordinary skill in the art would know how to make monoclonal antibodies to different regions p60 protein and identify the epitopes. It is routine in the art to make monoclonal antibodies (chapter 6 Harlow and Lane 1988) to various peptides including the one, which is claimed. The claimed invention is prima facie obvious in view of Kohler et al 1990 (Infection and Immunity, 58, 1943-1950) and Lerner or Harlow and Lane 1988 (Antibodies; Cold Spring Harbor) absent any convincing evidence to the contrary.

Applicants' arguments filed on 3/5/02 have been fully considered but they are not deemed to be persuasive.

Applicant argues that a skilled worker would not know from Kohler and Lerner which of the many possible p60 peptides to use as immunogen and references cited do not suggest or disclose the invention. Further, the applicant states the Declaration provided by Dr.Bubert and Dr Neumann support that it is extremely difficult to predict a particular peptide will have a structure that is suitable for generating antibody. The examiner disagrees with the applicant because generating antibodies to any given antigen or epitope in the recent years has become routine. Further, Campbell states " it is customary now for any group working on a macromolecule to clone the genes coding for it and make monoclonal antibodies to it (see Campbell, monoclonal antibody technology 1984, Chapter 1, page 29, under basic research)

Art Unit: 1645

without any clear objective" (i.e., no motivation needed to make antibodies). Further, Kohler et al suggests that the restriction fragment length polymorphism detected with the iap gene coding for p60 protein may be useful in identifying and distinguishing virulent *L.monocytogenes* strains. Therefore, it is obvious to make monoclonal antibodies to different epitopes of p60 protein and hence this rejection is maintained.

New Rejections Based on Amendment

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

6. Claims 42-43 and 50-70 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 42 and 43 rejected as being vague and unclear. Does the antibody claimed bind to all pathogenic *Listeria*? Does all pathogenic *Listeria* contain epitope SEQ.ID.NOS: 17, 20, 26, 29, 30 or 31?

Claim 63 is vague, confusing and not clear. Does applicant intend to mean an isolated antibody, which binds to an epitope from the group consisting essentially of SEQ.ID.NO: ---?

Claim 66 is vague, confusing and not clear. Does applicant intend to mean an isolated antibody ---- wherein said antibody does not cross react with any other epitope of p60 protein from other organisms?

Claim 69 is vague, confusing and not clear. Does applicant intend to mean a composition comprising----- binds to a different epitope of said peptides?

Claim 70 is vague, confusing and not clear. Does applicant intend to mean a composition comprising----- immunizing with different peptides from the group consisting of SEQ.ID.NOS: ----, or by immunizing with different said immunogenic conjugates comprising peptides from the group consisting of SEQ.ID.NOS: ----?

Status of Claims

7. No claims are allowed.

Conclusion

8. This application contains claims 39-41 and 44-49 are drawn to an invention non-elected with traverse in Paper No. 7. A complete reply to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.s

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP ' 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

Art Unit: 1645

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

5/23/02


LYNETTE R. F. SMITH
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